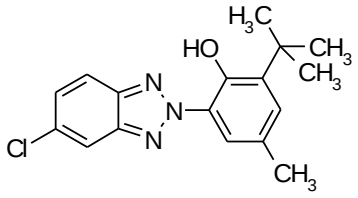
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	3896-11-5
Chemical Name	2-*tert*-Butyl-6-(5-chloro-2H-benzotriazol-2-yl)-4-methylphenol
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Physical-chemical properties

The substance is a pale yellow solid with a melting point of 139 °C, a boiling point of ≥ 300 °C and a calculated vapour pressure of 7.6E-07 Pa at 25 °C (MPBWIN v1.43). The calculated octanol-water partition coefficient (log k_{ow}) is 5.55 (KOWWIN v1.67) and the water solubility is < 1.0 mg/L at 20 °C.

Human Health

No information on toxicokinetics or metabolism is available.

The inhalation LC_{50} was > 270 mg/m^3 (the maximum attainable dust concentration) for 4-hr exposure in rats. There were no deaths during the study. Necropsy of all animals showed a slight amount of lung hyperemia. No other effects were noted. The oral [OECD TG 423] and dermal LD_{50} values in rats were > 2000 mg/kg bw. There were no deaths or clinical signs of systemic toxicity during the studies. No abnormalities were noted at necropsy in the oral study (necropsy was not performed in the dermal study).

The substance was not a skin or eye irritant. Some slight irritation, fully reversible within 72 hours, was observed in a skin irritation assay performed in rabbits. Mild conjunctivitis, fully reversible within 72 hours was observed in one animal out of six in an eye irritation assay performed in rabbits.

The substance was not skin sensitizing. A skin sensitization assay performed in guinea pigs and patch testing in humans were negative. The substance was not a photoallergen in guinea pigs.

The repeated dose toxicity of the substance has been investigated in four studies. In a repeated dose oral toxicity study in dogs the substance was administered via the diet to 5 animals/sex in the control and high dose groups and 4 animals/sex in the other dose groups at 0, 200, 1000 or 5000 ppm (equivalent to approximately 0, 6.2, 29.6 or 168 mg/kg bw/day for males and 0, 6.5, 32.2 or 153 mg/kg bw/day for females) for 13 weeks. One animal of each sex in the 0 and 5000 ppm groups were kept on the control diet for a further 4 weeks prior to sacrifice. All other animals were sacrificed at the end of the 13 week dosing period. No treatment-related deaths or clinical signs were observed in either sex. Treatment related effects (weight loss) were observed in females at 5000 ppm. Based on weight loss, the NOAEL for repeated dose oral toxicity is 1000 ppm (equivalent to 29.6 mg/kg bw/day for males and 32.2 mg/kg bw/day for females).

In a repeated dose oral toxicity study in rats [comparable to OECD TG 453] the substance was administered via the diet to 50 animals/sex/group at 0, 1000, 3000 or 10000 ppm (equivalent to approximately 0, 37.7, 113.2 or 382.6 mg/kg bw/day in males and 0, 50.4, 147.7 or 501.9 mg/kg bw/day in females) for 104 weeks. Based on a reduction in red cell parameters in males and females and bodyweight gain in males seen at 10000 ppm, the NOAEL for repeated dose toxicity is 3000 ppm (equivalent to 113.2 mg/kg bw/day for males and 147.7 mg/kg bw/day for females).

In a repeated dose oral toxicity study in mice [comparable to OECD TG 451] the substance was administered via the diet to 50 animals/sex/group at 0, 5, 50 or 500 mg/kg feed (equivalent to a mean daily intake of 0, 0.7, 6 and 62 mg/kg bw in males and 0, 0.7, 6 and 59 mg/kg bw in females) for 24 months. There were no treatment-related effects at any

dose. The NOAEL for repeated dose toxicity is 500 mg/kg feed, equivalent to 62 mg/kg bw/day in males and 59 mg/kg bw/day in females.

In a combined repeated dose toxicity study with reproduction/developmental toxicity screening test in rats [OECD TG 422] the substance was administered via gavage to 12 animals/sex/group at 0 (vehicle), 62.5, 250 or 1000 mg/kg bw/day. Recovery group females (6 animals/group) were dosed at 0 (vehicle), 250 or 1000 mg/kg bw/day. Males were dosed for a total of 42 days, from 14 days before mating, and females were dosed from 14 days before mating throughout the mating and pregnancy period to day 6 of lactation (44-56 days). There were no treatment-related effects at any dose in test or recovery group animals. The NOAEL for repeated dose toxicity in adult animals is 1000 mg/kg bw/day.

In a bacterial reverse mutation assay with multiple strains of *Salmonella typhimurium* and one strain of *Escherichia coli* [OECD TG 471], the substance was negative both with and without metabolic activation. An *in vitro* chromosomal aberration test in CHL cells [OECD TG 473] was negative with and without metabolic activation. *In vivo*, no evidence of a dominant lethal effect was observed in the offspring of male mice treated [comparable to OECD TG 478] with a single administration of the substance at 0, 1000 or 3000 mg/kg bw by gavage. The substance was not genotoxic in a bone marrow chromosome aberration test [comparable to OECD TG 475] or a micronucleus test [comparable to OECD TG 474] performed using Chinese hamsters dosed by gavage with the substance at 0, 500, 1000 or 2000 mg/kg bw/day on two consecutive days. Based on these results, the substance is considered to be non genotoxic *in vitro* and *in vivo*.

The carcinogenic potential of the substance has been investigated in two studies. In an oral study in rats [comparable to OECD TG 453] the substance was administered via the diet to 50 animals/sex/group at 0, 1000, 3000 or 10000 ppm (equivalent to approximately 0, 37.7, 113.2 or 382.6 mg/kg bw/day in males and 0, 50.4, 147.7 or 501.9 mg/kg bw/day in females) for 104 weeks. General toxicity effects are described in the repeat dose toxicity section above. There was no treatment related carcinogenic activity at any dose. In an oral study in mice [comparable to OECD TG 451] the substance was administered via diet to 50 animals/sex/group at non-toxic doses of 0, 5, 50 or 500 mg/kg feed (equivalent to a mean daily intake of 0, 0.7, 6 and 62 mg/kg bw in males and 0, 0.7, 6 and 59 mg/kg bw in females) for 24 months. There were no signs of general toxicity in this study and no treatment related carcinogenic activity at any dose. Based on these results the substance is considered to have no carcinogenic potential.

The reproductive toxicity of the substance has been investigated in the combined repeated dose toxicity study with reproduction/developmental toxicity screening test in rats [OECD TG 422] described above. No adverse effects on reproductive or developmental parameters were observed up to the highest dose tested. The NOAEL for reproductive/developmental toxicity in this combined study was considered to be 1000 mg/kg bw/day. The developmental toxicity of the substance has been investigated in prenatal developmental toxicity studies in rats and mice [comparable to OECD TG 414]. No evidence of developmental toxicity was observed in rats at doses up to 3000 mg/kg bw/day. In mice, there was a slight, but statistically significant, increase in the proportion of foetuses with incomplete ossification of sternebrae at a dose level of 3000 mg/kg bw/day, although the group mean foetal body weights were higher in the high dose group than controls. In rats and mice, no maternal toxicity was observed up to the highest dose tested, and no teratogenic effects were noted. The NOAELs for developmental toxicity from these studies in rats and mice are 3000 and 1000 mg/kg bw/day respectively. Based on these results, the overall NOAEL for reproductive /development toxicity of this substance is 1000 mg/kg bw/day.

Environment

The substance is not expected to be hydrolyzed under normal environmental conditions. In the atmosphere, indirect photo-oxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of 8.6 hours (AOPWIN v1.92). An aerobic biodegradation study [OECD TG 301B] resulted in 2-10 % biodegradation and a second study [modified MITI Test (I), OECD TG 301C] resulted in 0 % biodegradation after 28 days. The substance is not readily biodegradable under aerobic conditions. A Mackay level III fugacity model calculation with equal and continuous distributions to air, water and soil compartments suggests that the substance will distribute mainly to the soil (74.4 %) and sediment (19.5 %) compartments with minor distribution to the water compartment (6.1 %) and negligible amount in the air compartment. If released only to the air compartment, the substance will distribute mainly to the soil compartment (93.7 %) with minor distribution to the sediment compartment (4.8 %). If released to water, the substance will distribute mainly to the sediment (76.3 %) and water (23.7 %) compartments. If released to soil the substance stays in the soil compartment (99.9 %) with negligible amounts in other compartments. A calculated Henry's law constant of 1.19E-08 $Pa.m^3$/mole at 25 °C [HENRYWIN v3.20] suggests that volatilization of the substance from the water phase is not expected to be high. A log k_{oc} of 4.64 was estimated [KOCWIN v2.00] and

indicates a high potential for accumulation in soil.

Although a log K_{ow} of 5.55 was estimated [KOWWIN v1.67], the substance is expected to have some ~~low~~ potential for bioaccumulation in the aquatic environment based on measured bioconcentration factors of 196-802 (0.05 mg/L) and 548-895 (0.005 mg/L) from a study [OECD TG 305C] where common carp (*Cyprinus carpio*) were exposed to the substance for 8-10 weeks at 25 °C.

The following acute toxicity test results have been determined for aquatic species:

Fish [*Danio rerio*]	96 h LC_{50} > limit of water solubility.
Invertebrate [*Daphnia magna*]	24 h EC_{50} > limit of water solubility.
Algae [*Desmodesmus subspicatus*]	72 h E_bC_{50} > limit of water solubility (area under growth curve method).
Sewage sludge microorganisms	3 h IC_{50} > 100 mg/L (nominal)

The following chronic toxicity test results have been determined for aquatic species:

Algae [*Desmodesmus subspicatus*]	72 h NOE_bC > limit of water solubility

No information was identified concerning toxicity to soil or sediment-dwelling organisms.

Exposure

Annual domestic production and imported amounts in Japan was approximately 10 – 100 tonnes in 2003. Worldwide production volume is not available. The substance is used as a UV absorber for ink, paint, sealant, and plastics (mainly polyolefins and polyesters) used in, for example, building materials and automobile interior parts. It is also used as a UV filter for personal care formulations such as cosmetics and fragrance and is approved for use as an additive in food contact materials in the EU, Japan and US. The amount of the substance used in plastics is up to 0.5 %w/w. The substance may enter the environment at the production site and at chemical industries manufacturing the downstream products. Release to the environment from disposed products is limited due to its low water solubility. Release to the environment via wastewater is possible from its use in personal care products. Occupational exposure to the substance can occur mainly by inhalation and dermal routes at the production and user sites during operations. The atmospheric concentration was measured at one production site in Japan. A maximum concentration of 0.21 mg/m3 was recorded during removal of the product from the centrifuge however operators wear helmets, protective eye goggles and respirators during all operations in order to minimise their exposure to the substance. Consumer exposure to the substance can occur, mainly by the dermal route, through contact with a variety of finished products which contain the mixture. Some oral exposure may occur via migration into food from packaging.

RECOMMENDATIONS and RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health:

The chemical is currently of low priority for further work. The chemical is currently of low priority for further work because of its low hazard profile.

Environment:

The chemical is a candidate for further work. The chemical is a candidate for further work (not readily biodegradable, some potential for bioaccumulation). Further work recommended is a chronic toxicity study to sediment-dwelling organisms [OECD TG 218] as the sediment is the compartment most likely to be exposed.